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Original Article

Plasma folate status and dietary folate intake among Chinese women of childbearing age

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Abstract

Maternal folic acid deficiency is an underlying risk for neural tube defects (NTDs). China has one of the highest prevalences of NTDs, and the prevalence rates of NTDs vary by region. We characterized plasma folate level and dietary folate intake among Chinese women of childbearing age by region (North and South, East and West, urban and rural) to provide evidence for establishing policy to prevent NTDs. A total of 1003 women of childbearing age from five provinces in China were interviewed. Fasting blood samples were collected. Plasma folate concentrations were determined by a microbiological assay. Dietary intake data were collected using a 24-h recall. Both the plasma folate concentrations and dietary folate intake of women in the South (25.9 nmol L^{-1} and 211.0 μg day^{-1}) were higher than those of women in the North (13.3 nmol L^{-1} and 189.2 μg day^{-1}). In the North, plasma folate concentrations and dietary folate intake of women in rural areas were lower than those of women in urban areas, whereas, in the South, an opposite pattern was observed. No difference was found between women in the East and West, in either the North or South regions. Plasma folate and dietary folate intake among Chinese women of childbearing age were suboptimal and varied by region. Different folic acid supplementation approaches and dosage should be undertaken to improve folate status of women in different areas. Particular attention should be paid to women in the North, especially in northern rural areas.

Keywords: folate, folic acid, plasma folate status, dietary folate intake, women of childbearing age, neural tube defects.

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Introduction

Maternal folic acid deficiency was established as an underlying risk for neural tube defects (NTDs), and folic acid supplementation during the periconceptional period could reduce the risk of NTDs (MRC Vitamin Study Research Group 1991; Czeizel 1993; Berry *et al.* 1999). Many governments and organizations recommend that women of childbearing age take folic acid supplements daily (Van Allen *et al.* 1993; Centers for Disease Control and Prevention 1995; Institute of Medicine 1998; Rasmussen *et al.* 1998) and/or implement mandatory or voluntary food folic acid fortification to prevent NTDs (Food & Drug Administration 1996; Freire *et al.* 2000; Metz *et al.* 2002; Ray *et al.* 2002a).

China is among the high NTD-prevalent countries, and the birth prevalence rates of NTDs vary by region. Rates in southern China (about 5 per 10 000) were similar to those in developed countries, while rates in northern China (about 20 per 10 000), especially in Shanxi province (higher than 60 per 10 000), were the highest in the world (Dai *et al.* 2002; International Clearinghouse for Birth Defects Monitoring Systems 2004). Rates in rural areas were higher than those in urban areas (Xiao *et al.* 1990; Dai *et al.* 2002), and rates tended to decline from East to West (Xiao *et al.* 1990; Chinese Birth Defects Monitoring Collaborative Group 1992). The Chinese government has been considering undertaking strategies to reduce the occurrence of NTDs. In 1993, the Ministry of Health recommended women of childbearing age take 400 μg of folic acid daily (Department of Science, Technology and Education, Ministry of Health 1996). The government conducted a pilot study on fortifying flour with eight kinds of nutrients, including 200 μg folic acid per 100 g flour in some areas since 2002 (Chai 2006).

However, data on blood folate status and dietary folate intake of Chinese women of childbearing age are lacking. The few studies that reported the blood folate or dietary folate status of women in China were limited regionally to Beijing (Gao *et al.* 2003) and Shanxi (Li *et al.* 1996; Zhang *et al.* 2006; Ren *et al.* 2007), with very high prevalence of NTDs, or Shanghai (Shrubsole *et al.* 2001), Anqing (Ronnenberg *et al.* 2000) and Jiangsu (Li *et al.* 1996; Ren *et al.* 2007), with very low prevalence of NTDs, or focused on middle-aged and older women (Dyer *et al.* 2003; Hao *et al.* 2003). Existing evidence was insufficient to assess folate status among women of childbearing age countrywide. It would be a challenge for the Chinese government to make an appropriate policy to improve folate status among women of childbearing age and reduce NTDs nationwide without information on how folate status varies within the country.

The purpose of this paper was to characterize the plasma folate level and dietary folate intake among Chinese women of childbearing age by region (North and South, East and West, urban and rural), to provide evidence for establishing national policy to improve folate status among women of childbearing age and prevent NTD-affected pregnancies, as well as to provide baseline data for evaluating the impact of the intervention policy in the future.

Materials and methods

Subjects

As a part of the Study on Nutrition Status among Chinese Women of Childbearing Age, the present study was conducted in three northern provinces – Liaoning, Shandong and Gansu – and two southern provinces – Guangdong and Sichuan. In terms of approximate geographical location (Fig. 1), and for the purpose of analysis, we combined Liaoning and Shandong to represent northeast, Gansu to represent northwest, Guangdong to represent southeast, and Sichuan to represent southwest. In each province, we selected one city and one county, and from each, one community or village was selected as project sites. The socioeconomic status of the project site was representative of the provinces. Recruitment was conducted between April and May 2005. Using residential registration data, we identified eligible women in the communities or villages. The inclusion criteria of subjects were: (1) ages 18–30 years; (2) not pregnant or breastfeeding; and (3) free from hypertension, diabetes, cancer, and heart, liver, renal and gastrointestinal diseases, as well as other serious diseases. Each community or village had about 150 to 200 eligible women.

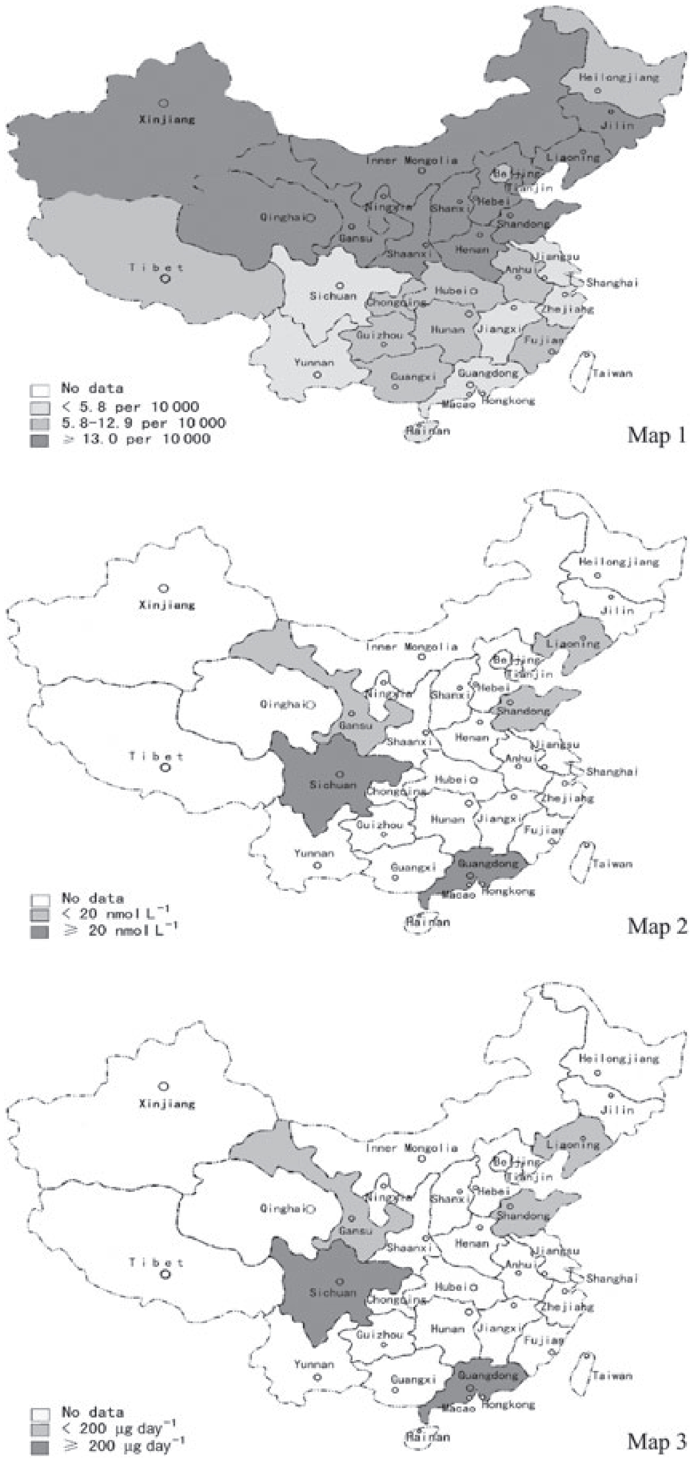

Fig. 1. Distributions of prevalence of neural tube defects (NTDs), plasma folate concentration and dietary folate intake in China. Map 1: Data of prevalences of NTDs are from the study of Dai and co-authors (Dai *et al.*, 2002). The cut-off values, 5.8 per 10 000 and 13.0 per 10 000, are the average prevalence rate of NTDs in the South and that in the whole of China. Maps 2 and 3: Data of plasma folate concentration and dietary folate intake are from our study. The cut-off values are established by us.

We distributed leaflets about the study to eligible women, informed and invited them to participate in the study, and took the first 100 women who consented. The Institutional Review Board of Peking University Health Science Center reviewed and approved the study protocol.

In order to achieve stable estimates of means of the studied nutrients, including folate and Vitamins A, B_6, and B_{12}, and to characterize the difference in means and deficient rates by region, based on estimates of means and deficient rates of the studied nutrients from previous studies in China, we calculated the sample size at the 0.05 significance level [95% confidence interval (CI)] and the statistical power of 90% to detect a minimum detectable difference as 15% of the estimates of studied nutrients. Finally, we determined to recruit 100 women from each site to meet the appropriate sample size for most studied nutrients (Zhang 2006).

Measurements

At the community health centre, a trained interviewer administered a structured questionnaire to collect subject information on sociodemographic and personal characteristics, comprising age, ethnicity, educational level, current cigarette and alcohol drinking, use of oral contraception, and use of folic acid supplements or multivitamins containing folic acid. Women's dietary data were collected using a 24-h recall. Folate values of foods were based on Chinese Food Composition (Yang 2005). Body weight in light clothing and height without shoes were measured to the nearest 0.1 kg and 0.1 cm with a beam weighing scale and a height scale, respectively. Body mass index (BMI) was calculated as weight (kg)/height $(m)^2$. A total of 9 mL overnight fasting blood was collected from each subject using venipuncture by a qualified nurse.

Blood samples were drawn into K3EDTA-containing Vacutainer tubes (Becton Dickinson, Franklin Lakes, NJ, USA) and centrifuged within 1 h of collection. Plasma and red blood cells were separated and frozen at −20°C. All specimens were transported on dry ice to the central laboratory of the Institute of Reproductive and Child Health, Peking University, and stored at −70°C before nutritional analyses. The plasma folate concentrations were determined by a microbiological assay (O'Broin & Kelleher 1992). The intra- and inter-assay coefficients of variation were less than 9% across the full range of folate concentrations.

Statistical analysis

All data summarization and analysis were performed using SPSS package for Windows, version 11.5 (SPPS, Chicago, IL, USA). As the distributions of plasma folate concentrations and dietary folate intake were positively skewed, natural logarithmic transformations were used to normalize the distributions, and inverse transformations were used to provide geometric means and their 95% CI. Folate deficiency was defined as plasma folate less than 6.8 nmol L^{-1} [from radioassay, i.e. 9.2 nmol L^{-1} converted to result of microbiological assay (see Note)] (Herbert & Das 1994). Chi-square test was used to compare deficient rates and linear regression analyses (using SPSS general linear models procedure) were conducted to compare means of plasma folate concentration and dietary folate intake (as the dependent variable, respectively) in the North vs. South, East vs. West and urban vs. rural (regions as the fixed factors), adjusted for potentially confounding variables (as the covariates), i.e. age, BMI, educational level, multivitamin and/or folic acid use. All P values were two-sided and statistical significance was set at $P \leq 0.05$.

Results

A total of 1008 women took part in the study. Three women whose blood samples were hemolytic and two women who did not complete dietary recall were excluded, leaving 1003 women (99.5%) for analysis. Demographic characteristics are shown in Table 1. The mean age of participants was 25.7 (±SD 3.3) years and mean BMI was 21.3 (±SD 2.8). The mean age and mean BMI differed between some regions. Most women (97.3%) were ethnic Han Chinese, and there were no marked regional differences. Most women (96.4%) finished middle school education or above; the distributions of level of education differed between some regions, but most notably between urban and rural. Use of cigarettes, alcohol and oral contraception were not prevalent among Chinese

Table 1. Characteristics of Chinese women of childbearing age in the study

Characteristic	South				North				Total
	East		West		East		West		
	Urban	Rural	Urban	Rural	Urban	Rural	Urban	Rural	
Number of women	100	100	100	100	201	202	100	100	1003
Age (years, mean ± SD)	25.1 ± 3.3	25.0 ± 3.2	23.2 ± 2.9	26.4 ± 2.6	26.0 ± 3.4	26.9 ± 2.9	25.3 ± 3.0	26.3 ± 3.5	25.7 ± 3.3
BMI (mean ± SD)	19.9 ± 2.4	21.4 ± 3.5	20.1 ± 2.3	21.3 ± 2.4	21.2 ± 2.4	22.9 ± 3.0	21.0 ± 2.6	20.9 ± 2.3	21.3 ± 2.8
Han ethnic group (%)	100.0	100.0	97.0	95.0	95.5	95.5	99.0	100.0	97.3
Level of education (%)									
Elementary	1.0	3.0	0.0	11.0	0.0	6.9	1.0	6.0	3.6
Middle School	6.0	66.0	11.1	79.0	2.0	73.8	4.0	48.0	36.7
High School	41.0	28.0	10.1	9.0	47.0	18.3	38.0	28.0	28.5
College and above	52.0	3.0	78.8	1.0	51.0	1.0	57.0	18.0	31.3
Current cigarette smoking (%)	2.0	0.0	3.0	2.0	1.0	5.4	1.0	1.0	2.2
Current alcohol drinking (%)	4.0	2.0	3.0	4.0	4.5	1.5	4.0	0.0	2.9
Oral contraception use (%)	3.0	0.0	1.0	0.0	1.5	2.5	0.0	0.0	1.2
Multivitamin and/or folic acid use (%)	6.0	1.0	8.0	0.0	3.0	0.5	4.0	4.0	3.0

women, being 2.2%, 2.9% and 1.2%, respectively, and did not vary between regions. Only 3.0% of women reported that they consumed folic acid supplement or multivitamins containing folic acid more than once per week in the past 3 months. The rates were no substantial differences between most regions.

Table 2 shows the mean plasma folate concentrations by region, and Figs 1 (map 2) and 2 are the corresponding graphical representation. The geometric mean of women living in the South was 25.9 nmol L^{-1} (95% CI: 24.7–27.1) and that of women living in the North was 13.3 nmol L^{-1} (95% CI: 12.8–13.7). In both urban and rural areas, and the East and West, women living in the South had higher plasma folate concentrations than those living in the North. After controlling for age, BMI, education level, and multivitamins and/or folic acid supplement use, the significant difference between southerners and northerners was unchanged. In the North, urban women had higher plasma folate concentrations than rural women, whereas in the South, urban women had lower plasma folate concentrations than rural women. Both in the North and South, there was no significant difference in plasma folate concentrations between the East and West.

Using 6.8 nmol L^{-1} as the cut-off value, 1.5% and 20.0% of the participants in the South and North were plasma folate deficient, respectively. The deficiency rates amongst women in the North, especially in the northeast (22.8%), were higher than those of women in the South. There was no significant difference in folate deficiency rates between urban and rural women in the southeast and northeast. In the southwest, the folate deficiency rate in the urban area (4.0%) was higher than that in the rural area (0.0%). But in the northwest, the deficiency rate in the rural area (20.0%) was higher than that in the urban area (9.0%).

Table 3 shows the mean dietary folate concentrations by region, and Figs 1 (map 3) and 3 are the corresponding graphical representations. The geometric mean of dietary folate intake of the subjects was 211.0 μg day^{-1} (95% CI: 201.3–221.1) in the South and 189.2 μg day^{-1} (95% CI: 181.8–196.9) in the North. Dietary folate intake of the southerners was higher than that of the northerners. After adjusting for women' s age, BMI, education level, and multivitamins and/or folic acid supplement use, the significant difference between southerners and northerners was unchanged. In the northwest,

Table 2. Plasma folate concentrations and folate deficient rates among Chinese women of childbearing age by region

Region	Geometric mean (95% CI, nmol L^{-1})		Deficient rate (%)†
	Crude	Adjusted*	
South, overall	25.9 (24.7–27.1)	26.2 (25.0–27.4)‡	1.5‡
East			
Overall	26.2 (24.7–27.8)	26.5 (24.9–28.2)‡	1.0‡
Urban	24.4 (22.2–26.9)	24.3 (22.1–26.6)‡§	2.0‡
Rural	28.1 (26.3–30.0)	28.8 (26.3–31.5)‡	0.0‡
West			
Overall	25.6 (23.9–27.4)	26.0 (24.4–27.7) ‡	2.0‡
Urban	22.4 (20.4–24.6)	23.2 (21.0–25.6)‡§	4.0§
Rural	29.3 (26.7–32.2)	29.1 (26.4–32.0) ‡	0.0‡
North, overall	13.3 (12.8–13.7)	13.6 (13.1–14.1)	20.0
East			
Overall	12.6 (12.0–13.1)	12.9 (12.4–13.4)	22.8¶
Urban	13.1 (12.3–13.9)	14.1 (13.1–14.7)§	19.4¶
Rural	12.1 (11.4–12.9)	11.5 (10.7–12.3)	26.1
West			
Overall	14.7 (13.8–15.7)	14.6 (13.7–15.6)	14.5
Urban	16.4 (15.0–18.0)	16.5 (15.1–18.1)§	9.0§
Rural	13.2 (12.1–14.4)	12.9 (11.8–14.1)	20.0

*Geometric means of plasma folate concentration were controlled for age, body mass index, education level and multivitamins and/or folic acid supplement use. †Folate deficiency rates using 6.8 nmol L^{-1} (from radioassay, i.e. 9.2 nmol L^{-1} converted to result of microbiological assay) as cut-off value. ‡$P < 0.01$ for the comparison with the North. §$P < 0.01$ for the comparison with rural areas in the same region. ¶$P < 0.01$ for the comparison with the west in the South/North.

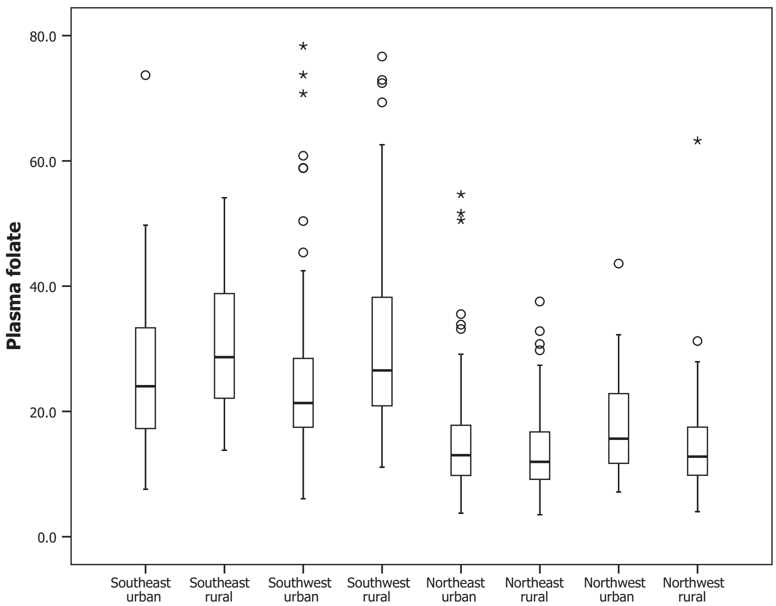

Fig. 2. Distribution of raw plasma folate concentrations among Chinese women of childbearing age by regions.

dietary intake of urban women was significantly higher than that of rural women. However, in the South, dietary intake of urban women was less than that of rural women but not to a statistically different degree. With the exception of lower dietary intake of rural women in the northwest compared with rural women in the northeast, there was no significant difference in dietary folate intake between

Table 3. Geometric mean of dietary folate intake among Chinese women of childbearing age by region (95% CI, μg day^{-1})

Region	Crude	Adjusted*
South, overall	211.0 (201.3–221.1)	212.9 (202.8–223.6)†
East		
Overall	213.7 (200.8–227.5)	215.1 (201.0–230.3)†
Urban	200.1 (182.2–219.7)	205.0 (185.5–226.5)
Rural	228.2 (210.3–247.5)	225.9 (204.7–249.3)†
West		
Overall	208.2 (194.1–223.4)	210.4 (196.4–225.5)†
Urban	205.5 (184.5–229.0)	201.4 (181.3–223.7)
Rural	211.0 (193.0–230.8)	220.8 (198.4–245.8)†
North, overall	189.2 (181.8–196.9)	188.0 (180.8–195.6)
East		
Overall	192.3 (183.5–201.4)	190.9 (181.8–200.4)
Urban	194.5 (180.7–209.5)	199.2 (185.3–214.2)
Rural	190.0 (179.5–201.2)	181.5 (167.9–196.2)‡
West		
Overall	183.2 (169.9–197.4)	182.7 (170.8–195.5)
Urban	203.9 (185.2–224.6)	211.2 (191.3–233.0)§
Rural	164.3 (147.0–183.7)	159.1 (144.5–175.3)

*Geometric means of dietary folate intake were controlled for age, body mass index, education level and multivitamins and/or folic acid supplement use. †$P < 0.01$ for the comparison with the North. ‡$P < 0.01$ for the comparison with the west in the South/North. §$P < 0.01$ for the comparison with rural areas in the same region.

women living in the East and those living in the West.

Discussion

This is the first large sample and broad coverage study to report plasma folate status and dietary folate intake among Chinese women of childbearing age. Also, for the first time in China, folate status, especially dietary folate intake among women of childbearing age, was characterized by region. Results of our study showed that the plasma folate status and dietary folate intake among Chinese women of childbearing age was far from optimal, especially among women living in northern China.

Results of our study showed that the plasma folate status among women of childbearing age in northern China was lower than that of women in southern China. The geometric mean concentration [13.3 nmol L^{-1} (95% CI: 12.8–13.7)] among women in northern China was about the mean concentration [9.7 ± 4.3 nmol L^{-1} from radioassay, i.e. 13.5 ± 5.6 nmol L^{-1} converted to result of microbiological assay] among Chilean women of childbearing age before flour fortification with 220 μg/100 g folic acid, but far lower than the mean (37.2 ± 9.5 nmol L^{-1} from radioassay, i.e. 59.1 ± 13.2 nmol L^{-1} converted to result of microbiological assay) among Chilean women after fortification (Hertrampf *et al.* 2003); lower than the median [4.8 ng mL^{-1} (95% CI: 4.5–3.4) from radioassay, i.e. 15.3 nmol L^{-1} (95% CI: 14.3–16.8) converted to result of microbiological assay] among women of childbearing age in the United States before cereal-grain fortification with 140 μg/100 g folic acid, lower than the 10th per centile [6.4 ng mL^{-1} (95% CI: 5.8–7.0) from radioassay, i.e. 21.0 nmol L^{-1} (95% CI: 18.9–23.2) converted to result of microbiological assay] among women in the United States after fortification (Centers for Disease Control and Prevention 2002). The geometric mean [25.9 nmol L^{-1} (95% CI: 24.7–27.1)] among women in southern China was higher than the mean concentration among Chilean women before flour fortification but lower than the mean among Chilean women after fortification. And it was about the 75th per centile [7.8 ng mL^{-1} (95% CI: 7.3–8.3) from radioassay, i.e. 26.1 nmol L^{-1} (95% CI: 24.3–28.0) converted to result of microbiological assay] among women in the United States before fortification, and was between the 10th and the 25th per centile [9.1 ng mL^{-1} (95% CI: 8.7–9.5) from radioassay, i.e. 30.9 nmol L^{-1} (95% CI: 29.4–32.4) converted to result of microbiological assay] of women in the United States after fortification (Centers for Disease Control and Prevention 2002). The deficient rates of plasma folate of the northerners were also higher than those of the southerners. Using 6.8 nmol L^{-1} (from radioassay, i.e. 9.2 nmol L^{-1} converted to result of microbiological assay) as the cut-off value, 20.0% and 1.5% of the participants in the North and South, respectively, were plasma folate deficient. Moreover, 65.9% and 12.0% of Chinese women of childbearing age in the North and South, respectively, did not achieve the serum folate levels (≥15.9 nmol L^{-1}) associated with very low risk for NTDs (Daly *et al.* 1995)

To our knowledge, no large sample dietary folate intake data amongst Chinese women of childbearing

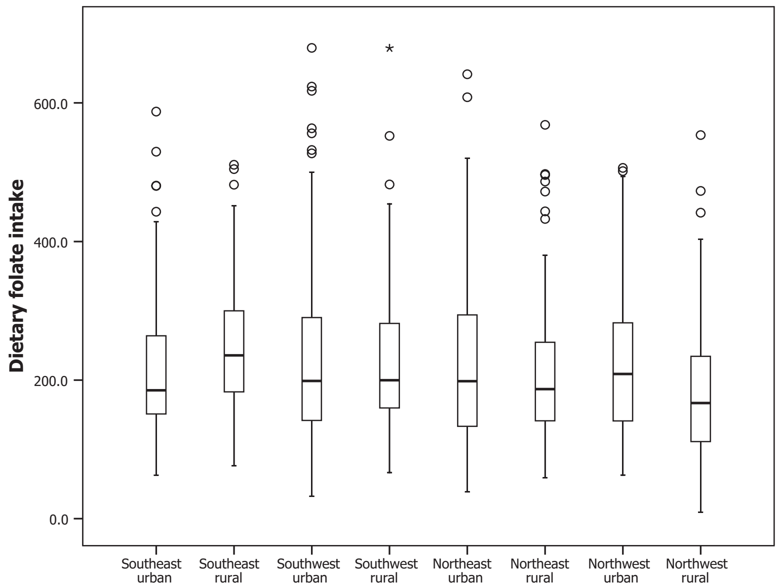

Fig. 3. Distribution of raw dietary folate intake among Chinese women of childbearing age by regions.

age have been reported. Our study showed that dietary folate intake amongst Chinese women of childbearing age was low. The geometric mean of total dietary folate intake amongst women of childbearing age in southern China was 211.0 μg day^{-1} (95% CI: 201.3–221.1). It was about the mean (217 ± 5.2 μg day^{-1}) of women at 20–39 years old in the United States before fortification, but less than the mean (294 ± 12.6 μg day^{-1}) of women at 20–39 years old in the United States after fortification (Dietrich *et al.* 2005). The geometric mean of total dietary folate intake among women of childbearing age in northern China was 189.2 μg day^{-1} (95% CI: 181.8–196.9). It was less than the mean of women at 20–39 years old in the United States before fortification and after fortification. The distribution of dietary folate intake of the subjects was similar to the distribution of the plasma folate concentration: dietary folate intake among women in the North was less than in the South, with urban northerners higher than rural northerners, urban southerners lower than rural southerners, and in either the North or South regions, there was no significant difference between east and west. However, we found that the difference in dietary folate intake was not as significant as plasma folate concentrations between women in different areas. For example, plasma folate concentration of women in the South was 1.9 times that of women in the North, but the dietary folate intake of women in the South was only 1.1 times that of women in the North. Several factors may be contributory. First, some kinds of green vegetables consumed frequently by the women in the South are special local products. We could not determine their folate content from the Chinese Food Composition Table, and so we estimated them using the average folate content of vegetables. This might be an underestimation, resulting in the dietary folate intake of women in the South being underestimated on the whole. Second, analysis of food sources of dietary intake showed that women in the South obtained folate mainly from vegetables and fruits, while women in the North obtained folate mainly from grains. Cooking, processing and storage can destroy some folate in food (Chinese Nutrition Society 2000). Grains are often stored, cooked and processed more extensively than vegetables and fruits, thus the lower actual folate intake for women in the North than in the South. Third, although most (97.3%) women in the study were of Han ethnicity, genetic backgrounds might still play a role. Studies shown that Han populations in the North had a higher frequency of a mutation in the gene encoding methylenetetrahydrofolate reductase enzyme (MTHFR) than those in the South (Wilcken *et al.* 2003; Zhu *et al.*

2006), and the mutated form of MTHFR is associated with decreased plasma concentrations (Molloy *et al.* 1997). The low plasma folate concentration in women in the North may be partly attributable to their higher frequency of MTHFR mutation.

Results of our study showed that the geographical distributions of plasma folate and dietary folate intake among Chinese women of childbearing age were inversely associated with the distributions of birth prevalence rates of NTDs between North and South China (Xiao *et al.* 1990; Berry *et al.* 1999; Dai *et al.* 2002) (Fig. 1). It confirmed the negative association between maternal folate status and occurrence of NTDs. Moreover, Xiao *et al.* suggested that the prevalence of NTDs tended to decline from east to west in China (Xiao *et al.* 1990; Chinese Birth Defects Monitoring Collaborative Group 1992). For the first time, we compared the plasma folate concentrations and dietary folate intake between women in the east and west. Results showed neither plasma folate concentration nor dietary folate intake among women in the east and west, in either the North or South regions, had significant difference. We reviewed articles on the prevalence of NTDs in China. No other article compared prevalence of NTDs in the East with that in the West. Using data on NTD prevalence of each province in China reported by Dai *et al.* (2002), we did not find the trend Xiao *et al.* (1990) reported. Further studies are needed to clarify the distribution of NTD prevalence and folate status among people in the East and West of China.

As mentioned earlier, our studies showed that folate status of Chinese women of childbearing age was far from optimal for preventing NTDs. Hence, many women, especially those living in the North, would enter pregnancy with severely compromised folate status. Increasing dietary folate intake and improving blood folate status among Chinese women of childbearing age are urgent. Studies suggested a substantial increase in women's blood folate status (Lawrence *et al.* 1999; Ray *et al.* 2002b; Hertrampf *et al.* 2003) and a significant decrease in the risk of NTDs (Honein *et al.* 2001; Gucciardi *et al.* 2002; Persad *et al.* 2002; Ray *et al.* 2002a; Williams *et al.* 2002; De Wals *et al.* 2003; Hertrampf & Cortes 2004; Lopez-Camelo *et al.* 2005) after folic acid fortification in the United States, Canada and Chile. The effectiveness of folic acid fortification was striking. Fortifying food with folic acid may also be an effective approach to improving the suboptimal folate status of women in China. The Chinese government has conducted pilot studies on food fortification since 2002. However, according to the result of our study, two problems should be noted before popularizing food fortification with folic acid in China. One issue is the different baseline levels of folate status between women in South and North China. Our study showed the geometric mean concentration of plasma folate among women of childbearing age in Northern China was near the median among women of childbearing age in the United States before fortification, and that among women in southern China was near two times that of women in the North, higher than the 75th per centile among women in the United States before fortification and near the 25th per centile after fortification. It indicated that fortifying food with the 200 μg/100 g dosage, which is higher than the 140 μg/100 g dosage used in the United States, would be appropriate for northerners, whereas it might be excessive for southerners. Although folic acid is generally regarded as safe, with some studies suggesting that folic acid intake may also reduce the risk of other kinds of birth defects, such as oral–facial clefts (Goh *et al.* 2006; Badovinac *et al.* 2007) and congenital heart diseases (Goh *et al.* 2006), stroke (Wang *et al.* 2007), breast cancer (Ericson *et al.* 2007), colorectal cancer (Sanjoaquin *et al.* 2005) and neuroblastoma (Olshan *et al.* 2002; French *et al.* 2003), other studies suggested that consuming supplements containing folic acid or food fortified with folic acid may increase the risk of certain kinds of cancer (Cole *et al.* 2007; Mason *et al.* 2007). Morris *et al.* (2007) suggested that in seniors with low vitamin B_{12} status, high serum folate was associated with anaemia and cognitive impairment (Morris *et al.* 2007). Hao *et al.* reported that 5.5% of Chinese adults were deficient in vitamin B_{12} (Hao *et al.* 2004). Vitamin B_{12} was not included in the fortification formula in China (Chai 2006). Although the role that folate plays in cancer development and its association with anaemia and cognitive impairment in seniors need to be proven, we should be mindful that more folate is not better in all circumstances and folic acid fortification may have adverse effects in subpopulation groups not originally targeted for fortification, and use care in developing public health policy (Kim 2004; Ulrich 2007; Ulrich & Potter 2007). Much attention and further study are needed to establish the appropriate folic acid dosages for food fortification in different areas of China to maximize effective prevention while avoiding potential adverse effects. The other problem is the inherent difficulty with implementing food fortification in China. Presently, only a few large- or medium-sized mills participate in the national flour fortification programme, producing 1 million tons of fortified flour yearly, which accounts for less than 1% of total flour output in China and covers only 7.7‰ of the Chinese population (Chai 2006). In rural areas, most people bring their own grain to mills, preferring to produce and eat their own flour (Zhang *et al.* 2006). It is difficult to spread fortified flour throughout China in a short period. Before fortified food is widely available and acceptable all over the country, it is necessary to undertake some measures to promote periconceptional folic acid supplements for NTD prevention among Chinese women of childbearing age, especially those living in the northern rural.

A limitation of this study was the sample size was too small for some purpose. One hundred women from each project site met the recommended minimum sample size needed to achieve stable estimates of means of the studied nutrients and to characterize the difference in means and deficient rates by regions. However, 100 participants did not meet the appropriate sample size to estimate plasma folate deficient rates in the South (≥496), to compare deficient rates between urban and rural in the North (≥153) and to compare plasma folate deficient rates between rural and urban in the South (≥286). In addition, a 24-h recall was used to obtain dietary folate intake data in this study. Although the 24-h recall method is the most often used dietary assessment tool in large clinical studies, such as the National Health and Nutrition Examination Surveys and Nationwide Food Consumption Survey in the United States, a 24-h recall is not an ideal methodology to assess individuals' dietary nutrients intake but is more suitable to assess dietary intake of a population with a large sample size (Buzzard 1998). By and large, the method was appropriate to the purpose of our study, i.e. assessing the folate intake among women in different regions. However, it was insufficient to assess each individual's dietary intake or to assess whether an individual reaches the recommended nutrient intake. More studies using 24 h recall and other dietary intake assessment methods are needed to evaluate the results of our study and to estimate dietary folate intake among Chinese people.

In conclusion, the present study suggests that plasma folate and dietary folate intake among Chinese women of childbearing age were suboptimal and varied by region. Different folic acid supplementation approaches and different folic acid dosage for food fortification should be undertaken to improve folate status of women in different areas to prevent NTDs and avoid potential adverse effects. Particular attention should be paid to women in the North, especially rural women. To ensure preventive effects before food fortification is implemented all over the country, the Chinese government and health care staff should undertake measures to encourage women of childbearing age to consume 400 μg of folic acid daily.

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Note

The Bio-Rad QuantaPhase II radioassay (BR) and microbiological assay (MA) are the two principal methods used to measure plasma and red blood cell folate. Studies showed that the radioassay produces lower results than microbiological assay. To compare the results of our study from MA with that from radioassay in the United States, we converted results from BR to MA using the equation established by Fazili *et al.* [$\log_{10}$ MA = 0.0504 + (1.0958 × $\log_{10}$ BR) + (0.6358 × IND) − (0.4105 × IND × $\log_{10}$ BR), IND = 0 for BR results ≤ 45 nmol L^{-1} and IND = 1 for BR results ≥ 45 nmol L^{-1} and IND-1 for BR results ≥ 45 nmol L^{-1}] (Fazili *et al.* 2007).

Key messages

- Maternal folic acid deficiency is an underlying risk for neural tube defects (NTDs). China is among the high NTD-prevalent countries, and the prevalence rates of NTDs vary by region.
- This study showed plasma folate concentrations and dietary folate intake among Chinese women of childbearing age were suboptimal and varied by region.
- Plasma folate concentrations and dietary folate intake of women in the South were higher than those of women in the North.
- In the North, plasma folate concentrations and dietary folate intake of women in rural areas was lower than those of women in urban areas, whereas, in the South, an opposite pattern was observed.
- In China, different folic acid supplementation approaches and dosage should be undertaken to improve folate status of women in different areas.

Conflicts of interest

None declared.

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